

PATENT

Attorney Docket No. 33568/US/DJB  
Attorney Matter No. 465377-01102  
Application No. 10/778,010

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Srinivasan *et al.*

Application No. 10/778,010

Filed: February 11, 2004

For: Ion Exchange Particle-Bound Flow-  
Through Porous Monolith

Art Unit: 1723

Examiner: Therkorn, Ernest G.

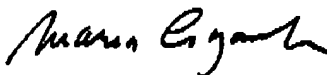
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**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

Sir:

Applicants request review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reasons stated below.

The undersigned is an attorney of record.

In an effort to reduce the issues for appeal, the following remarks are limited to the rejection of Claims 1-6 and 10 under 35 U.S.C. 103(a) as being unpatentable over Sherrington (U.S. Patent No. 5,066,784) in view of Barretto (U.S. Patent No. 5,532,279) and will not address the rejection of Claim 3 further in view of Pohl (U.S. Patent No. 5,376,047).

**REMARKS**

By way of introduction, Claim 1 recites:

Flow-through ion exchange medium comprising a monolithic stationary phase having interconnecting pores defined by pore walls, and fine ion exchange polymeric layering particles irreversibly bound directly or indirectly to the pore walls.

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The product has the advantages set forth in paragraph [0044] – [0046] including an ability to control capacity and selectivity in a monolith in a reproducible medium. The uniformity of the coating process leads to high chromatographic separation efficiencies.

The Examiner asserts that the claims differ from Sherrington in reciting polymeric layering particles and that Barretto discloses multiple layers of layering particles to allow more control over column capacity and improve column capacity. The Examiner further asserts that this disclosure in Barretto provides the motivation for the combination. Thus, the Examiner concludes that it would have been obvious to use layering particles in Sherrington. (See Office Action dated March 10, 2006.)

The Examiner further suggests that Sherrington discloses how to incorporate a gel into a monolith and that such gel would cause negligible pressure development during the flow of liquid through it. Thus, the Examiner concludes that, since there is no difference in pressure drops of liquid flow-through between the product disclosed in Sherrington and that of the claims, there are no unexpected results in the claimed product. (See the March 10, 2006 Office Action.)

Applicants respectfully disagree with the Examiner. In finding that Sherrington teaches (1) a monolithic stationary phase with gel in its interconnecting pores useful as an ion exchange medium, and (2) that such a gel-containing monolith would have negligible back pressure, the Examiner has made clear errors of fact. Based on these and the other errors set forth herein, the Examiner has failed to set forth a *prima facie* case of obviousness.

***Sherrington Disclosure***

Almost the entire disclosure of Sherrington is directed to porous polymeric particulate substrates with gel in the pores of the particles for peptides synthesis. Only two isolated sentences in Sherrington (Col. 2, lines 65-68, and Col. 4, lines 63-65) suggest that the substrate could be a monolithic block form. The Examiner notes the Sherrington disclosure at Col. 6, lines 25-32, that the gel causes negligible pressure development. However, the only detailed description of the product, set forth in the examples immediately following this statement, is of a milled and sieved powder as the substrate, not a monolith.

Sherrington refers to U.S. Patent No. 4,522,953 for suitable porous materials to be used as a substrate (Sherrington, Col. 4, line 48). As set forth in the '953 patent, such porous substrates are made by a process termed high internal phase emulsion (HIPE). Such polymers are not suitable for use as a monolith for binding gel as clearly set forth in U.S. Patent No. 6,100,306. At Col. 2, lines 16-38, the '306 patent states (1) HIPE polymers produce a block of polymer material the size and shape of the vessel used for polymerization; (2) it is very difficult to wash unpolymerized emulsion components out of the block;

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(3) the material can only be used by grinding the block into particles which is costly; (4) the size of the particles are limited; (5) removal of residual emulsion components is essential for many applications; and (6) no cost effective method for performing this wash step to remove the emulsion has been developed. Further, without washing the unpolymerized emulsion, such components would remain in the pores of the block and would create massive back pressure during chromatographic separation using such material as an ion exchange medium. Also, the residual unpolymerized emulsion likely would lead to significant errors in a chromatography run since the displaced emulsion components would contaminate the results. (See Request for Reconsideration, page 4.)

***Barretto Disclosure***

Barretto only discloses the use of layering particles on particulate substrates (beads) for a packed bed. In an analytical column packed with beads coated with layering particles, the liquid flows primarily through the interstices volume unoccupied by the beads, rather than flowing through the pores of the beads. In contrast, in a monolithic phase, the monolith pores are the only available flow path and so the entire liquid flow path is through the pores. Thus, the flow profile through monolithic pores is fundamentally different than flow through the interstices between the particles of the Barretto approach. Due to the primary liquid flow through the pores the mass transfer properties are improved for the monolithic phases particularly at high flow rates.

***Errors of Fact in Construing Sherrington***

For the foregoing reasons, Applicants respectfully submit that the Examiner has made clear errors of fact. Specifically, the Examiner concludes that Sherrington fairly discloses a gel-filled monolith which is useful as an ion exchange material and that such gel-filled monolith would provide negligible back pressure when used as an ion exchange medium. To the contrary, for the reasons set forth above, Sherrington does not disclose an effective monolith infused with a gel. The residual emulsion components in the pores would block penetration of the gel and thus inhibit binding of the gel or the layering particles of the present invention. Further, the block of the material disclosed in Sherrington must be ground into particles. Assuming the block could be used at all, such emulsion components would create massive back pressure. Further, such components likely would lead to significant errors when used as an ion exchange medium, e.g., for use in chromatographic analysis, because they would be displaced into the analyte solution and interfere with detection of analytes during a run.

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As set forth above, the Examiner's comment that Sherrington (Col. 6, lines 25-32) would suggest a negligible pressure development by infused gel relates to a particular bed of milled and sieved powder, not a monolith. The back pressure statement precedes the examples in which such a milled and sieved powder is used. Further, as set forth above, Sherrington teaches no practical way to use a monolith as a substrate for the gel.

***Elements of a Prima Facie Case of Obviousness***

To establish a *prima facie* case of obviousness, three basic criteria must be met, namely, (1) some suggestion or motivation to combine the reference teachings, (2) a reasonable expectation of success, and (3) the references must teach or suggest all of the claim limitations. M.P.E.P. § 2142. Applicants respectfully submit that the Examiner has failed to set forth a *prima facie* case of obviousness because the Examiner has failed to provide proper motivation to combine the prior art of record, and has failed to provide a reasonable expectation of success.

***No Motivation to Combine Exists***

As set forth above, the disclosure of Sherrington and Barretto are significantly different. The only motivation asserted by the Examiner for the combination is that Barretto discloses the use of multiple layers of layering particles to allow more control over column capacity and improved column capacity. However, that statement is the context of layering particulate substrates not monoliths. It does not provide motivation to substitute layering particles for a gel in the pores of a monolith. Further, the only monolith disclosure in Sherrington is in passing in two sentences. Monoliths have been available for many years (e.g., Ferchet U.S. Patent No. 5,334,310 cited at paragraph 3 of the specification), yet there is no suggestion to irreversibly bond layering particles to the pore walls of a monolith or that such a product would solve the problems of Sherrington or the advantages described above.

***No Reasonable Expectation of Success Exists***

Further, there is no reasonable expectation of success. For the reasons set forth above, the substrate materials of Sherrington could not be used in monolithic form as flow-through ion exchange medium as set forth in claim 1. Instead, the Sherrington material must be ground to fine particles for such use. Further, even if such materials could be used in a monolith form, residual emulsion components would fill the pores to inhibit the gel to fill the pores and would lead to interfere with the chromatographic analysis. Finally, the limited two-sentence disclosure of monoliths provides no guidance as to how to irreversibly bind a gel in the pores of a monolith.

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**CONCLUSION**

Applicants respectfully request that the Panel reconsider and withdraw the rejections over Sherrington in view of Barretto.

If the Examiner or the Panel believe, for any reason, that personal communication will expedite prosecution of this application, the Examiner and the Panel are invited to telephone the undersigned at the number provided below.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extension of time, and/or credit any overpayment to Deposit Account No. 50-2319 (Order No. 465377-1102; Docket No. 33568/US/DJB).

Prompt and favorable consideration of this Request is respectfully requested.

Respectfully submitted,

Dated: 8/10/06

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